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Editorial

"Modern" dermatopathology: facts and fictions

Light microscopic evaluation of formalin-fixed, paraffin embedded sections stained with Haematoxylin and Eosin (H&E) is the oldest tool used in dermatopathology and histopathology. It stands the challenge of time and is still the 'gold standard' for histopathological diagnosis in most situations. At roughly the same time, 'special' stains using different histochemical reactions to produce colour products were developed. Special stains are now used in looking for organisms (Ziehl Neelsen, Wade Fite, Grocott, Gram and Warthin-Starry stains), determining nature of deposits (Masson Fontana for melanin, Perl for iron, Congo red and others for amyloid, and various types of mucin stains), and high-lighting different cell types and components of the tissue (trichrome stain for collagen and elastic tissue, periodic acid Schiff for basement membrane material, toludine blue for mast cells). These special stains were found to be invaluable adjuncts to the 'routine' H&E stain.

Along with the development of special stains, other new techniques also emerged. These included electron microscopy, immunohistochemistry and molecular technique. The application of electron microscopy in ultrastructural analysis of various forms of epidermolysis bullosa remains unsurpassed but its original application in looking for subcellular detail had been replaced by immunohistochemistry and molecular techniques. Immunohistochemical techniques based on the affinity between animal antibodies raised against human antigen in diagnostic pathology was the most important advance in pathology in the last 50 years. Due to its simplicity and clean background, immunofluorescence (IF) is widely used to evaluate immunobullous disease and detecting lupus band since detailed morphology of structures being stained up is not required. In other occasions, IF technique is replaced by the two-stage immunohistochemistry employing some amplification system and colour product because correlation with light microscopic features (such as size, shape and nuclear morphology) and antigen expression can be made. With the development in antigen retrieval techniques, practically all antibodies useful for diagnostic purposes can work on formalin fixed paraffin embedded tissues and fresh tissue is no longer a necessity. It was this last advance that led to information explosion in the field of immunohistochemistry as research can be done on historical material. In dermatopathology, IF is essential in work up of bullous disease. However, its role in connective tissue disease and vasculitides are limited as many a time the findings are inconclusive or are not value added. For example, many cases of lupus erythematosus do not have the lupus band in lesional skin in our locality. On the other hand, 20% of specimen from sun exposed skin in healthy adults can have lupus band. In the field of vasculitides, diagnosis depends on the H&E finding of vasculitis. Although it is said to be useful in the diagnosis of Henoch Scholein purpura, our experience indicates that the IgA staining is either negative or weak. Therefore, the information gained is at most supportive given an appropriate clinical setting. While immunohistochemical techniques on paraffin sections are widely used in histopathology, they are infrequently employed in dermatopathology, and is mainly used for evaluating lymphoproliferative

disorders like lymphomatoid papulosis and cutaneous lymphoma. In mycosis fungicides (MF), my experience with the aberrant loss of CD5, CD7 and determining CD4/CD8 ratio is disappointing since most of the time they generate equivocal results for those early cases. Therefore, diagnosis of MF still relies on H&E morphology. One would also like to see more applications in diagnosing skin adnexal tumours but data so far does not provide breakthrough that makes immunohistochemistry part and partial for routine assessment of skin adnexal tumour.

Molecular technique is becoming more and more important in the field of hereditary disease, infectious disease and tumour pathology after the development of polymerase chain reaction (PCR). Although PCR is still best used on fresh tissue, formalin fixed paraffin embedded material can also be used if the segment of genetic material being studied is not too long. It is very useful in evaluating infectious disease because genomic material that normally does not exist in human tissue is the target for detection. In tumour pathology, we can either look for specific mutation of a tumour (especially in the field of sarcomas like synovial sarcoma), look for evidence of clonality of a proliferation (especially in B and T cell lymphomas), look for deletion of tumour suppressor gene by the "loss of heterozygosity" method, and look for effect of impaired DNA repair in many carcinoma syndromes such as microsatellite instability in Torre-Muir syndrome. Hereditary diseases impose the most difficult area for pathological study for they are rare and apparently homogeneous entities can be genetically heterogeneous. With advancement in molecular technique, we may eventually be possible to better classify genodermatosis by accurately delineating the underlying genetic defects.

It is always fascinating looking at all these 'hi-tech' advances. However, like all laboratory investigations, problems with false negative and false positive results undermine their diagnostic value. The importance of evaluating findings in light of clinical settings can never be over-emphasised. For example, in the study of early mycosis fungoides, given the sparse infiltrate of lymphoid cells, it is possible that only a few among all the lymphocytes belonging to a same clone can produce a clonal band in the gel after power amplification by PCR. We cannot conclude from this "pseudo-clone" that all the lymphocytes in the section belong to one clone. Another word of caution is that all these techniques are relatively new in comparison with the time honoured H&E method where our experience of clinical importance based on. At this moment, it is inappropriate for dermatologists and dermatopathologists to extrapolate the experience derived from the traditional diagnostic methods onto the finding using these new techniques.

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